sulfate content in buffer A. Impurities and thrombin fragments were to a large extent removed in the flow-through or in the wash fractions.

Please replace the paragraph at page 8, lines 15-26, with the following:

The thrombin fraction was loaded without further treatment directly onto a cation exchange column (CEC; in this case: FRACTOGEL® EMD SO_3, manufacturer: Merck, Darmstadt, Germany) equilibrated with buffer A, washed with equilibration buffer A and eluted by a gradient from 0 to 1.0 mol/l sodium chloride in buffer A. During the separation, final byproducts and thrombin fragments were removed so that the resulting α-thrombin eluate had a high specific purity of about 3500 IU/mg (protein determination by determining the absorption at 280 nm and using the conversion factor of 1.74 for a 0.1% strength solution in accordance with J.W. Fenton, II, M.J. Fasco, A.B. Stackrow, D.L. Aronson, A.M. Young and J.S. Finlayson, Human Thrombins. J Biol Chem 252; 3587-3598 (1977)). Table 1 shows the results of this thrombin purification and the resulting specific activity.

Please replace the paragraph at page 9, lines 3-14, with the following:

Starting from a thrombin concentrate of moderate or low purity, two chromatography steps were carried out. Initially the thrombin solution was mixed with 0.6 mol/l sodium sulfate and adsorbed onto a hydrophobic interaction chromatography (HIC) gel (in this case: Phenyl-Sepharose HP, manufacturer:

phosphate 0.1% PEG pH 6.5; (in this case PEG 6000, but other molecular weight

ranges can also be employed)) containing 0.6 mol/l sodium sulfate. After washing with buffer B containing 0.6 mol/l sodium sulfate, the bound thrombin was eluted by a gradient with decreasing sodium sulfate content in buffer B. Impurities and thrombin fragments were to a large extent removed in the flow-through or in the wash fractions.

Please replace the paragraph at page 9, lines 15-19, and page 10, lines 1-3, with the following:

The thrombin fraction was loaded without further treatment directly onto a cation exchange column (CEC; in this case: FRACTOGEL® EMD SO_3, manufacturer: Merck, Darmstadt, Germany) equilibrated with buffer C (10 mmol/Na phosphate, 166 mmol/l L-arginine pH 6.5), washed with equilibration buffer C and eluted by a gradient from 0 to 1.0 mol/l sodium chloride in buffer C. During the separation, final byproducts and thrombin fragments were removed so that the resulting α-thrombin eluate had a high specific purity of about 3300 IU/mg (cf. Table 2).

Please replace the paragraph at page 10, lines 15-16, and page 11, lines 1-7, with the following:

Starting from a thrombin eluate purified as in Examples 1 to 3 and after hydrophobic interaction chromatography and cation exchange chromatography, a filtration was carried out on a membrane with a small pore size (e.g. PLANOVA™ 15 nm). Even small viruses such as parvoviruses can be effectively removed with this

good yields in terms of thrombin activity and protein were obtained, with a good filtration